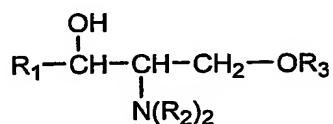


**CLAIMS:**

1. A stable lipid assembly comprising:
  - (a) a biologically active lipid having a hydrophobic region and a polar headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is less than 0.3;
  - (b) a lipopolymer having a hydrophobic lipid region and a polymer headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is at least 1.5.
2. The lipid assembly of Claim 1, comprising a lipid matrix, the lipid matrix comprising a lipid or a combination of lipids having an additive packing parameter in the range of 0.74-1.0.
3. The lipid assembly of Claim 1 or 2, having a level of water tightly bound to said lipopolymer headgroup of at least about 60 molecules of water per lipopolymer headgroup.
4. The lipid assembly of any one of Claims 1-3, wherein said biologically active lipid has a packing parameter which is greater than 1.
5. The lipid assembly of any one of Claims 1-4, wherein said biologically active lipid is selected from ceramides, ceramines, sphingamines, sphinganine-1-phosphate, di- or tri-alkylsphingosines and their structural analogs.
6. The lipid assembly of Claim 1 or 5, wherein said biologically active lipid has the following general formula (I):



wherein

- R<sub>1</sub> represent a C<sub>2</sub>-C<sub>26</sub>, saturated or unsaturated, branched or unbranched,

aliphatic chain, the aliphatic chain may be substituted with one or more hydroxyl or cycloalkyl groups and may consist of a cycloalkylene moiety;

- $R_2$  which may be the same or different, represents a hydrogen, a  $C_1$ - $C_{26}$  saturated or unsaturated, branched or unbranched chain selected from aliphatic, aliphatic carbonyl; a cycloalkylene-containing aliphatic chain, the aliphatic chain may be substituted with an aryl, arylalkyl or arylalkenyl group;
- $R_3$  represents a hydrogen, a methyl, ethyl, ethenyl or a phosphate group.

7. The lipid assembly of Claim 6, wherein said biologically active lipid is a  $C_2$ - $C_{26}$  ceramide.

8. The lipid assembly of Claim 6, wherein said biologically active lipid is N,N-dimethylsphingosine (DMS).

9. The lipid assembly of Claim 1, wherein said polymer headgroup has an atomic mass of at least 750 Da.

10. The lipid assembly of Claims 1 or 9, wherein said lipopolymer comprises a polymer headgroup selected from polyethylene glycol (PEG), polysialic acid, polylactic acid, polyglycolic acid, apolylactic-polyglycolic acid, polyvinyl alcohol, polyvinylpyrrolidone, polymethoxazoline, polyethyloxazoline, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyaspartamide, polyhydroxypropyl methacrylamide, polymethacrylamide, polydimethylacrylamide, polyvinylmethylether, polyhydroxyethyl acrylate, derivatized celluloses.

11. The lipid assembly of Claim 10, wherein said polymer headgroup is polyethylene glycol (PEG).

12. The lipid assembly of Claim 11, wherein said PEG has an atomic mass in the range of about 750Da to about 20,000 Da.

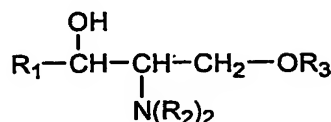
13. The lipid assembly of Claim 12, wherein said PEG has an atomic mass of 2,000Da ( $^{2k}$ PEG).

14. The lipid assembly of Claim 2, wherein said lipid matrix comprises a phospholipid.
15. The lipid assembly of Claim 14, wherein said phospholipid is a glycerophospholipid.
16. The lipid assembly of Claim 15, wherein said glycerophospholipid is selected from phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidic acid (PA), phosphatidylinositol (PI), phosphatidylserine (PS) and sphingomyelin (SPM) and derivatives of the same.
17. The lipid assembly of any one of Claims 2, 14-16, wherein said lipid matrix comprises a cationic lipid.
18. The lipid assembly of Claim 17, wherein said cationic lipid is a monocationic lipid having a headgroup selected from 1,2-dimyristoyl-3-trimethylammonium propane (DMTAP) 1,2-dioleyloxy-3-(trimethylamino) propane (DOTAP); N-[1-(2,3,-ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide (DMRIE); N-[1-(2,3,-dioleyloxy)propyl]-N,N-dimethyl-N-hydroxy ethyl- ammonium bromide (DORIE); N-[1-(2,3-dioleyloxy) propyl]-N,N,N- trimethylammonium chloride (DOTMA);  $3\beta$ [N-(N',N'- dimethylaminoethane) carbamoyl] cholesterol (DC-Chol); and dimethyl-dioctadecylammonium (DDAB).
19. The lipid assembly of Claim 18, wherein said cationic lipid is a polycationic lipid having a headgroup selected from spermine or spermidine.
20. The lipid assembly of Claim 19, wherein said polycationic lipid is N-[2-[[2,5-bis[3-aminopropyl)amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-1-propanaminium (DOSPA) or ceramide carbamoyl spermine (CCS).
21. The lipid assembly of any one of Claims 1-20, in the form of micelle.
22. The lipid assembly of any one of Claims 2-20, in the form of a liposome.
23. The lipid assembly of any one of Claims 1 to 22, comprising a targeting

substance associated with said lipid assembly.

24. The lipid assembly of Claim 23, wherein said targeting substance is an antibody, a functional fragment of an antibody, a cell-surface recognition molecule.
25. The lipid assembly of any one of Claims 1 to 24, associated with a therapeutically active agent.
26. A pharmaceutical composition comprising an amount of a stable lipid assembly, the amount being sufficient to achieve a biological effect at a target site, the lipid assembly comprising:
  - (a) a biologically active lipid having a hydrophobic region and a polar headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is less than 0.3;
  - (b) a lipopolymer having a hydrophobic lipid region and a polymer headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is at least 1.5.
27. The pharmaceutical composition of Claim 26, comprising a physiologically acceptable carrier.
28. The pharmaceutical composition of Claim 26, wherein said lipid assembly comprises a lipid matrix, the lipid matrix comprising a lipid or a combination of lipids having each a packing parameter in the range of 0.74-1.0.
29. The pharmaceutical composition of Claim 26, wherein the lipopolymer has a level of water tightly bound to its head-group of at least about 60 molecules of water per polymer headgroup.
30. The pharmaceutical composition of any one of Claims 26-29, wherein said biologically active lipid has a packing parameter which is greater than 1.
31. The pharmaceutical composition of any one of Claims 26-30, wherein said biologically active lipid is selected from ceramides, ceramines, sphingamines, sphinganine-1-phosphate, di- or tri-alkylsphingosines and their structural analogs.

32. The pharmaceutical composition of Claim 26 or 31, wherein said biologically active lipid has the following general formula (I):



wherein

- $\text{R}_1$  represent a  $\text{C}_2\text{-C}_{26}$ , saturated or unsaturated, branched or unbranched, aliphatic chain, the aliphatic chain may be substituted with one or more hydroxyl or cycloalkyl groups and may consist of a cycloalkylene moiety;
- $\text{R}_2$  which may be the same or different, represents a hydrogen, a  $\text{C}_1\text{-C}_{26}$  saturated or unsaturated, branched or unbranched chain selected from aliphatic, aliphatic carbonyl; a cycloalkylene-containing aliphatic chain, the aliphatic chain may be substituted with an aryl, arylalkyl or arylalkenyl group;
- $\text{R}_3$  represents a hydrogen, a methyl, ethyl, ethenyl or a phosphate group.

33. The pharmaceutical composition of Claim 31 or 32, wherein said biologically active lipid is a  $\text{C}_2\text{-C}_{26}$  ceramide.

34. The pharmaceutical composition of Claim 31 or 32, wherein said biologically active lipid is N,N-dimethylsphingosine (DMS).

35. The pharmaceutical composition of Claim 26, wherein the polymer headgroup has an atomic mass of at least 750 Da.

36. The pharmaceutical composition of Claim 26 or 35, wherein said lipopolymer comprises a polymer headgroup selected from polyethylene glycol (PEG), polysialic acid, polylactic acid, polyglycolic acid, apolylactic-polyglycolic acid, polyvinyl alcohol, polyvinylpyrrolidone, polymethoxazoline, polyethyloxazoline, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyaspartamide, polyhydroxypropyl methacrylamide, polymethacrylamide, polydimethylacrylamide,

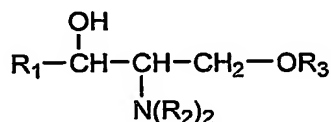
polyvinylmethylether, polyhydroxyethyl acrylate, derivatized celluloses.

37. The pharmaceutical composition of Claim 36, wherein said lipopolymer comprises a polyethylene glycol (PEG) headgroup.
38. The pharmaceutical composition of Claim 37, wherein said PEG has an atomic mass in the range of about 750 Da to about 20,000 Da.
39. The pharmaceutical composition of Claim 38, wherein said PEG has an atomic mass of 2,000Da (<sup>2k</sup>PEG).
40. The pharmaceutical composition of Claim 27, wherein said lipid matrix comprises a phospholipid.
41. The pharmaceutical composition of Claim 40, wherein said phospholipid is a glycerophospholipid.
42. The pharmaceutical composition of Claim 41, wherein said glycerophospholipid is selected from phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidic acid (PA), phosphatidylinositol (PI), phosphatidylserine (PS) and sphingomyelin (SM) and derivatives of the same.
43. The pharmaceutical composition of any one of Claims 27, 40-42, wherein said lipid matrix comprises a monocationic or polycationic lipid.
44. The pharmaceutical composition of Claim 43, wherein said monocationic lipid comprises a headgroup selected from 1,2-dimyristoyl-3-trimethylammonium propane (DMTAP) 1,2-dioleyloxy-3-(trimethylamino) propane (DOTAP); N-[1-(2,3,-ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide (DMRIE); N-[1-(2,3,-dioleyloxy)propyl]-N,N-dimethyl-N-hydroxy ethyl- ammonium bromide (DORIE); N-[1-(2,3-dioleyloxy) propyl]-N,N,N- trimethylammonium chloride (DOTMA); 3β[N-(N',N'- dimethylaminoethane) carbamoyl] cholesterol (DC-Chol); and dimethyl-dioctadecylammonium (DDAB).
45. The pharmaceutical composition of Claim 43, wherein said polycationic lipid comprises a cationic headgroup selected from spermine or spermidine.

46. The pharmaceutical composition of Claim 45, wherein said polycationic lipid is N-[2-[[[2,5-bis[3-aminopropyl]amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-1-propanaminium (DOSPA) or ceramide carbamoyl spermine (CCS).
47. The pharmaceutical composition of any one of Claims 26-46, wherein said lipid assembly is in a form of micelle.
48. The pharmaceutical composition of any one of Claims 26-47, wherein said lipid assembly is in a form of a liposome.
49. The pharmaceutical composition of any one of Claims 26-48, comprising a targeting substance associated with the assembly.
50. The pharmaceutical composition of Claim 49, wherein said targeting substance is an antibody, a functional fragment of an antibody, a cell-surface recognition molecule.
51. The pharmaceutical composition of any one of Claims 26-50, comprising a therapeutically active agent.
52. The pharmaceutical composition of any one of Claims 26-51, for the treatment of a disease, disorder or pathological condition.
53. The pharmaceutical composition of any one of Claims 26-52, for inhibiting cell proliferation.
54. A method for the treatment or prevention of a disease, disorder or pathological condition comprising providing an individual in need of said treatment, in a manner so as to achieve a therapeutic effect, an effective amount of a stable lipid assembly comprising:
- (a) a biologically active lipid having a hydrophobic region and a polar headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is less than 0.3;
  - (b) a lipopolymer having a hydrophobic lipid region and a polymer

headgroup, wherein the atomic mass ratio between the headgroup and hydrophobic region is at least 1.5.

55. The method of Claim 54, wherein said lipid assembly comprises a lipid matrix, the lipid matrix comprising a lipid or a combination of lipids having each a packing parameter in the range of 0.74-1.0.
56. The method of Claim 54 or 55, having a level of water tightly bound to the polymer headgroup of at least about 60 molecules of water per polymer headgroup.
57. The method of any one of Claims 54-56, wherein the biologically active lipid has a packing parameter which is greater than 1.
58. The method of any one of Claims 54-57, wherein said biologically active lipid is selected from ceramides, ceramines, sphinganine, sphinganine-1-phosphate, di- or tri-alkylsphingosines and their structural analogs.
59. The method of Claim 54 or 58, wherein said biologically active lipid has the following general formula (I):



wherein

- $\text{R}_1$  represent a  $\text{C}_2$ - $\text{C}_{26}$ , saturated or unsaturated, branched or unbranched, aliphatic chain, the aliphatic chain may be substituted with one or more hydroxyl or cycloalkyl groups and may consist of a cycloalkylene moiety;
- $\text{R}_2$  which may be the same or different, represents a hydrogen, a  $\text{C}_1$ - $\text{C}_{26}$  saturated or unsaturated, branched or unbranched chain selected from aliphatic, aliphatic carbonyl; a cycloalkylene-containing aliphatic chain, the aliphatic chain may be substituted with an aryl, arylalkyl or arylalkenyl group;
- $\text{R}_3$  represents a hydrogen, a methyl, ethyl, ethenyl or a phosphate group.



60. The method of Claim 58 or 59, wherein said biologically active lipid is a  $C_2$ - $C_{26}$  ceramide.
61. The method of Claim 58, wherein said biologically active lipid is N,N-dimethylsphingosine (DMS).
62. The method of Claim 54, wherein said polymer headgroup has an atomic mass of at least 750 Da.
63. The method of Claim 54 or 62, wherein said lipopolymer comprises a polymer headgroup selected from polyethylene glycol (PEG), polysialic acid, polylactic acid, polyglycolic acid, apolylactic-polyglycolic acid, polyvinyl alcohol, polyvinylpyrrolidone, polymethoxazoline, polyethyloxazoline, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyaspartamide, polyhydroxypropyl methacrylamide, polymethacrylamide, polydimethylacrylamide, polyvinylmethylether, polyhydroxyethyl acrylate, derivatized celluloses.
64. The method of Claim 63, wherein said polymer headgroup is polyethylene glycol (PEG).
65. The method of Claim 64, wherein said PEG has an atomic mass in the range of about 750Da to about 20,000 Da.
66. The method of Claim 65, wherein said PEG has an atomic mass of 2,000Da ( $^{2k}$ PEG).
67. The method of Claim 55, wherein said lipid matrix comprises a phospholipid.
68. The method of Claim 67, wherein said phospholipid is a glycerophospholipid.
69. The method of Claim 68, wherein said glycerophospholipid is selected from phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidic acid (PA), phosphatidylinositol (PI), phosphatidylserine (PS) and sphingomyelin (SM) and derivatives of the same.
70. The method of any one of Claims 55, 67-69, wherein said lipid matrix comprises a cationic lipid.

71. The lipid assembly of Claim 70, wherein said cationic lipid is a monocationic lipid having a headgroup selected from 1,2-dimyristoyl-3-trimethylammonium propane (DMTAP) 1,2-dioleyloxy-3-(trimethylamino) propane (DOTAP); N-[1-(2,3,-ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide (DMRIE); N-[1-(2,3,-dioleyloxy)propyl]-N,N-dimethyl-N-hydroxy ethyl- ammonium bromide (DORIE); N-[1-(2,3-dioleyloxy) propyl]-N,N,N- trimethylammonium chloride (DOTMA);  $3\beta$ [N-(N',N'- dimethylaminoethane) carbamoyl] cholesterol (DC-Chol); and dimethyl-dioctadecylammonium (DDAB).
72. The method of Claim 70, wherein said cationic lipid is a polycationic lipid having a headgroup selected from spermine or spermidine.
73. The method of Claim 72, wherein said polycationic lipid is N-[2-[[2,5-bis[3-aminopropyl]amino]-1-oxopentyl]amino]ethyl]-N,N-dimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-1-propanaminium (DOSPA) or ceramide carbamoyl spermine.
74. The method of any one of Claims 54-73, wherein said lipid assembly is in a form of a micelle.
75. The method of any one of Claims 54-73, wherein said lipid assembly is in a form of a liposome.
76. The method of any one of Claims 54-75, comprising administering said lipid assembly in association with a targeting substance.
77. The method of any one of Claims 54-76, comprising administering said lipid assembly in combination with a therapeutically active agent.
78. The method of Claim 77, wherein said therapeutically active agent is provided to said individual concomitant, before or after administration of said lipid assembly.
79. The method of any one of Claims 54-78, wherein said therapeutic effect comprises inhibition of cell proliferation.
80. The method of Claim 79, for the treatment of cancer.